Hemostasis in Uremia:
Bleeding Diathesis Vs. Hypercoagulability

Urology and Nephrology Center

Hussein Sheashaa, MD, FACP

Professor of Nephrology, Urology and Nephrology Center and Director of Medical E-Learning Unit, Mansoura University, and Executive Director of ESNT- Virtual Academy:
http://lms.mans.edu.eg/esnt/

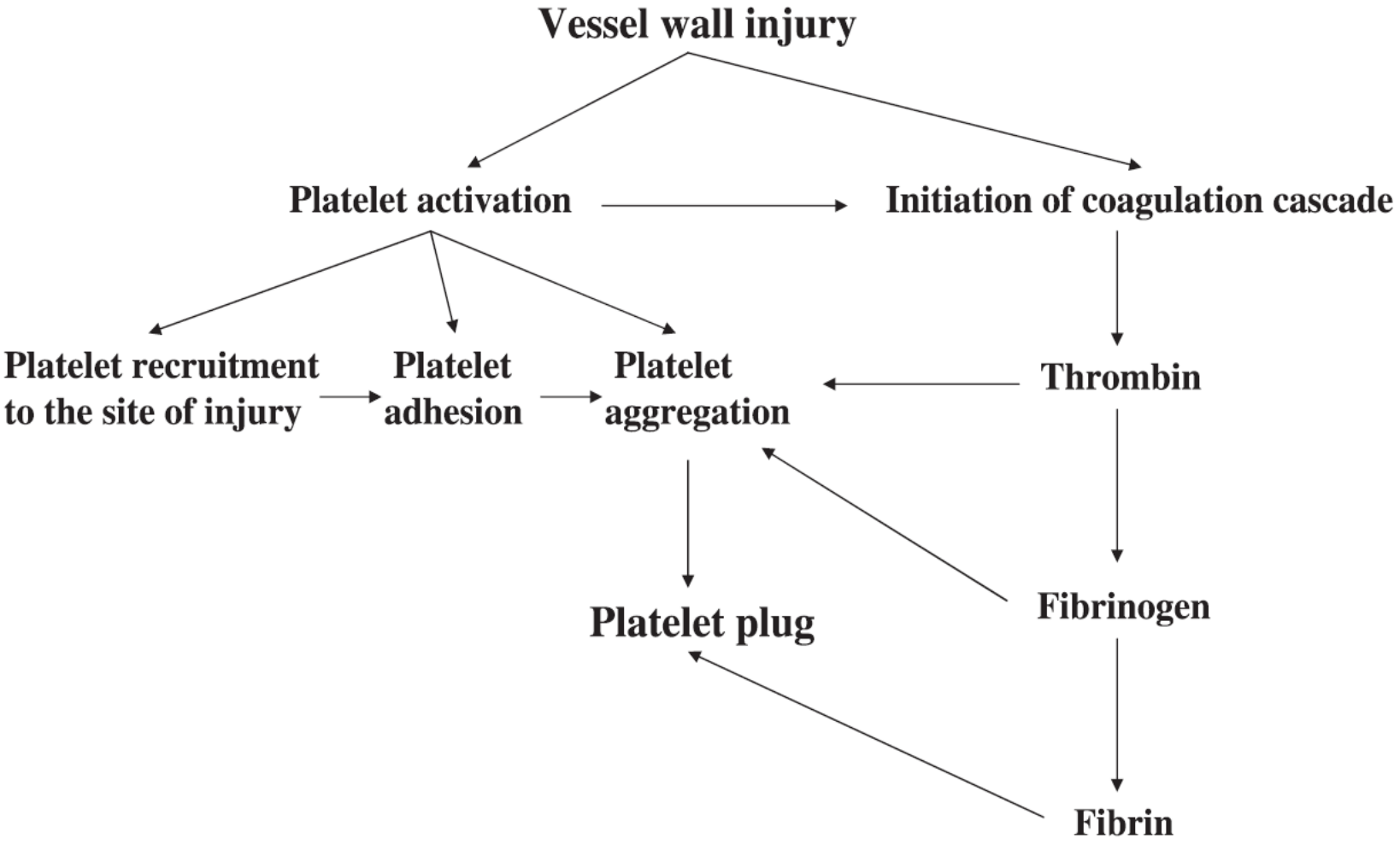
Tanta, July 28th, 2016

Urology and Nephrology Center

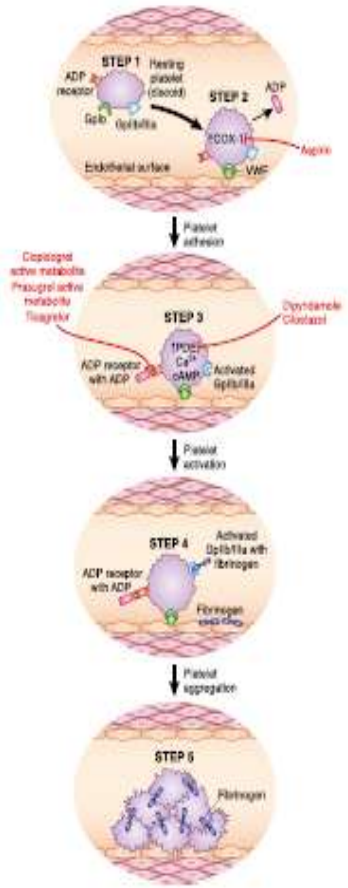
Outline

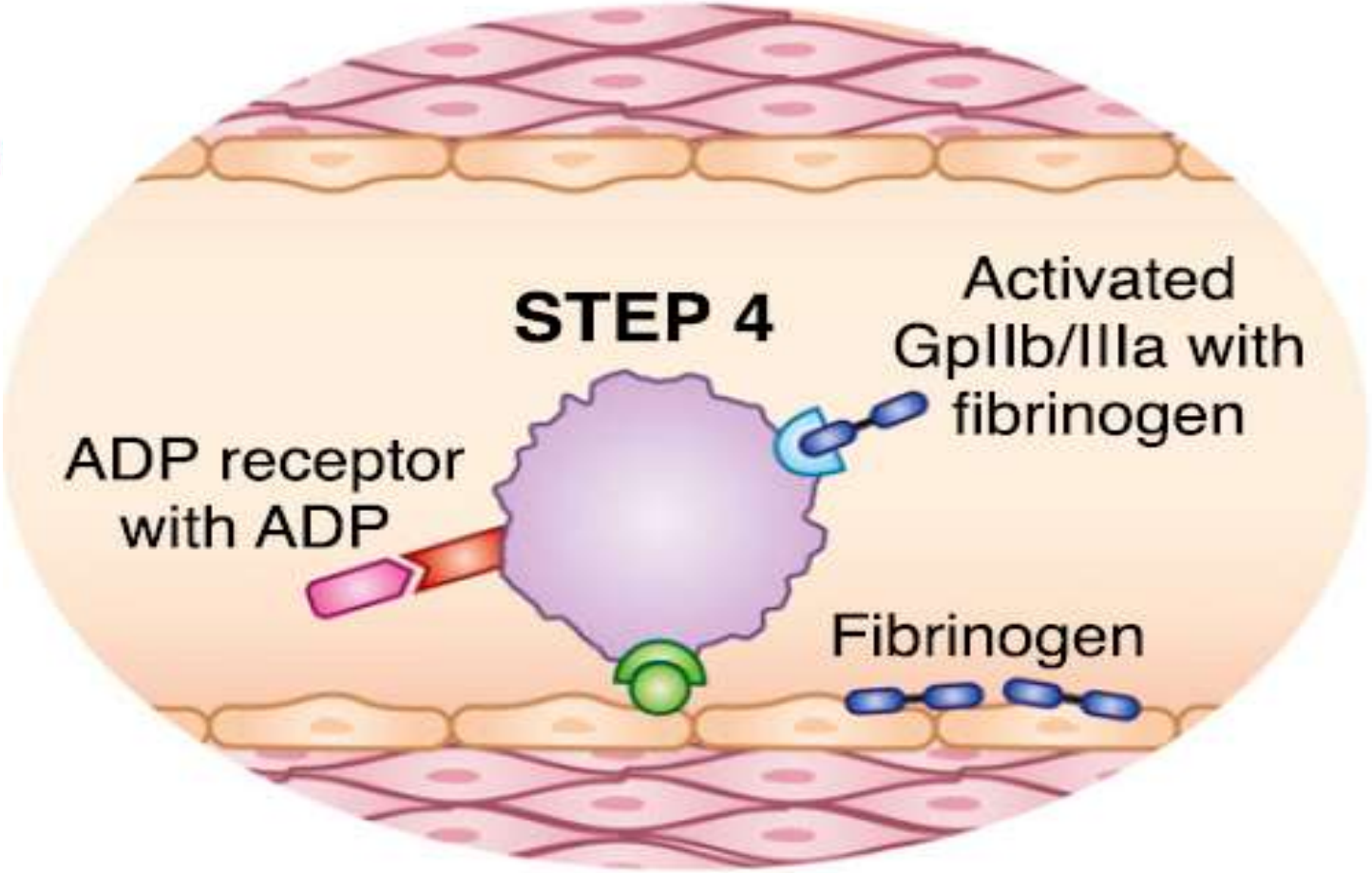
- Normal hemostasis
- Uremic bleeding
- Uremic thrombosis
- Therapeutics
- Closing

Normal Hemostasis



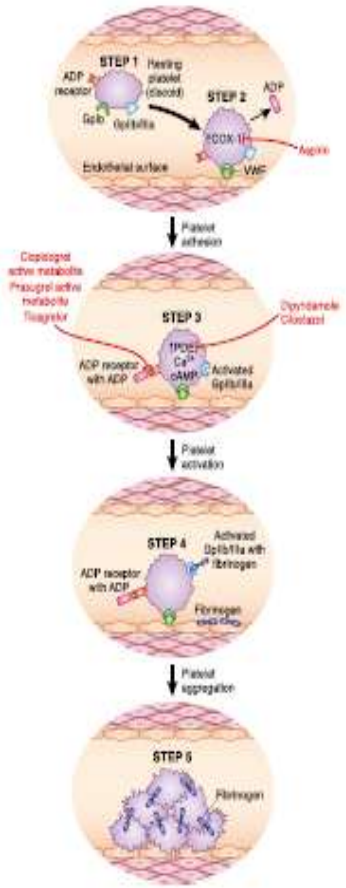
Steps of Platelet Activation and Aggregation

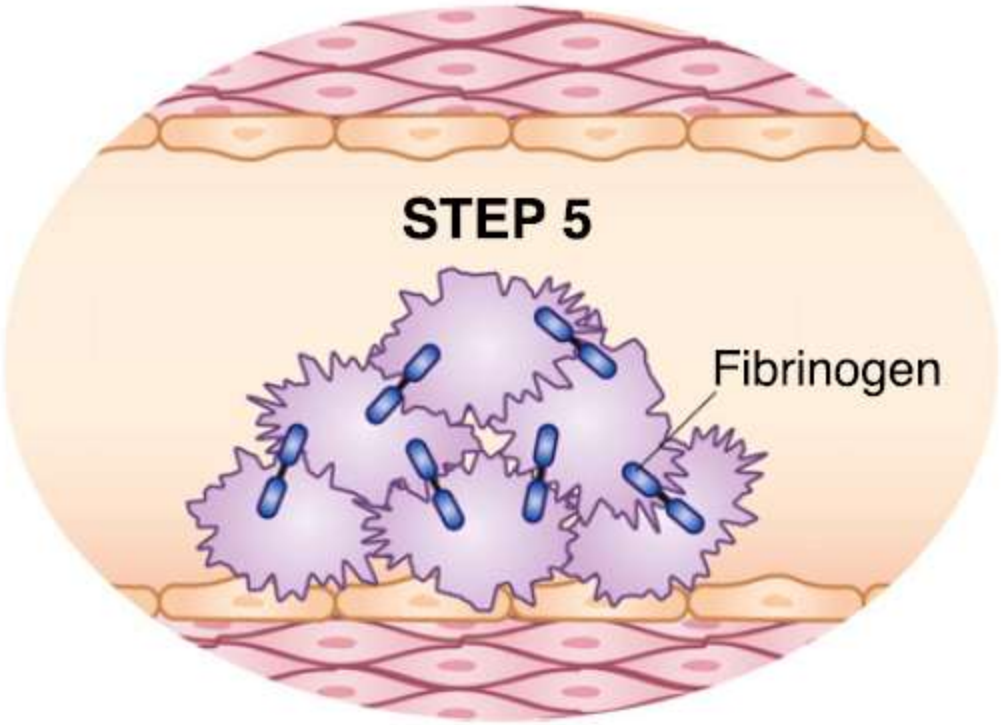




Clin J Am Soc Nephrol 8: 665–674, April, 2013

Steps of Platelet Activation and Aggregation





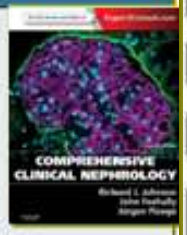
Clin J Am Soc Nephrol 8: 665–674, April, 2013

Increased Bleeding Events in Patients with CKD5D

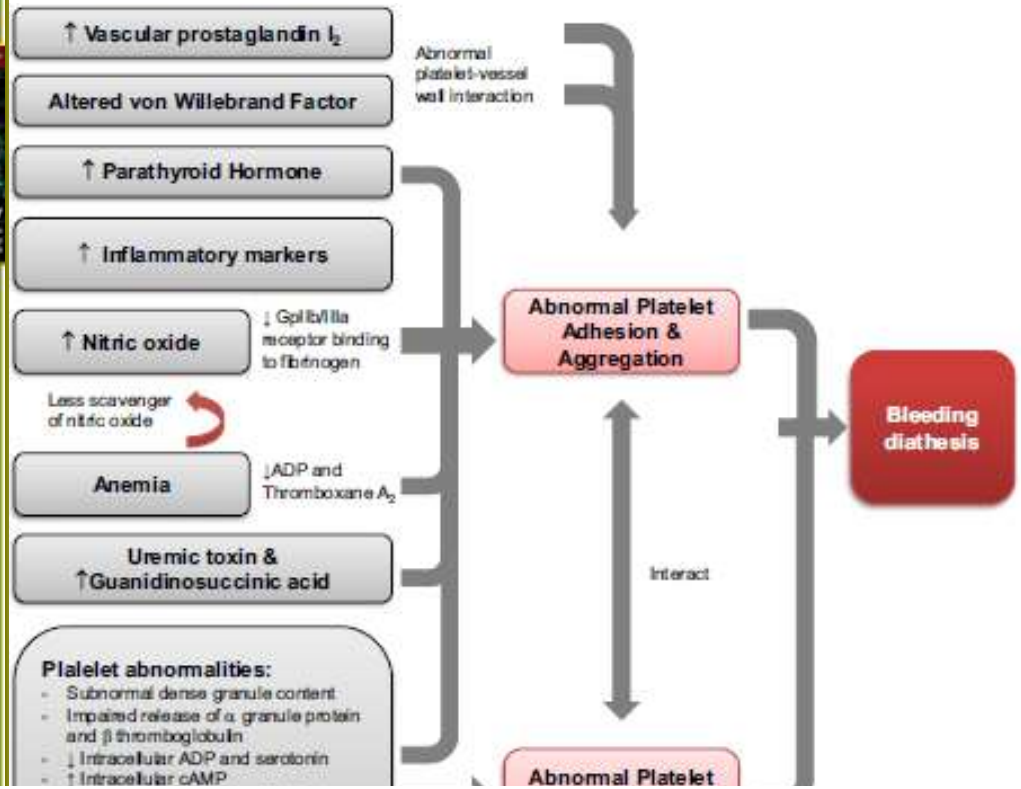
Urology and Nephrology Center

DNG Dalvandan Nephrology Group

Pathogenesis of Platelet Dysfunction in Uremia



- Platelet abnormalities
  - Alterations in membrane fluidity
  - Reduction in intracellular ADP and serotonin
  - Enhanced intracellular cAMP
  - Impaired release of β-thromboglobulin and ATP
  - Increased NO production
  - Increased intracellular Ca^{2+} (caused by secondary hyperparathyroidism)
  - Abnormal mobilization of platelet Ca^{2+}
  - Defective cyclooxygenase activity
  - Reduced thromboxane A_2 generation
  - Decreased platelet factor 3 availability
  - Reduced total GPIb content (with increased glycocalicin formation)
  - Reduced GPIIb/IIIa after stimulation
  - Diminished responsiveness to platelet agonists
  - Decreased clot retraction
  - Aggregation abnormalities (mostly hyperaggregation)
  - Abnormal platelet adherence
- Uremic toxins
- Anemia
- vWF abnormalities
- Vessel abnormalities
- Drugs (β-lactam antibiotics, nonsteroidal anti-inflammatory drugs, antiplatelet agents)



NDT Plus (2011) 4: 270–272
doi: 10.1093/ndtplus/sfr046
Advance Access publication 12 April 2011

Teaching Point
(Section Editor: A. Meyrier)

There's something fishy about this bleeding

NDT PLUS
Nephrology Dialysis Transplantation

Omega-3 FA

Uremic Bleeding: Prediction

Urology and Nephrology Center

The HAS-BLED Score to Assess 1-Year Risk of Major Bleeding in Patient With AF

HAS-BLED score

Condition	Points
H - Hypertension	1
A - Abnormal renal or liver function (1 point each)	1 or 2
S - Stroke	1
B - Bleeding	1
L - Labile INRs	1
E - Elderly (> 65 years)	1
D - Drugs or alcohol (1 point each)	1 or 2

HAS-BLED score	Bleeds per 100 patient-years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.70
5	12.5

Pisters R et al. Chest 2010;138(5):1093-1100.

Uremic Bleeding: Prediction

Urology and Nephrology Center

Curriculum in Cardiology

The atrial fibrillation conundrum in dialysis patients

An S. De Vriese, MD, PhD,[a] Rogier Caluwé, MD,[b] and Paolo Raggi, MD, PhD[c] *Brugge, Belgium; OLVZ Aalst, and Alberta, Canada*

Bleeding risk scores

Score acronym (reference)	Components	High risk
Modified Outpatient Bleeding Risk Index (mOBRI)	Age >65 y (1), history of stroke (1), history of gastrointestinal bleeding (1), recent myocardial infarction (1), Hct <30% (1), Cr >1.5 mg/dL (1), diabetes (1)	Score ≥4
HEMORR$_2$HAGES	Hepatic or renal disease (1), ethanol abuse (1), malignancy (1), age ≥75 y (1), reduced platelet count or function (1), rebleeding risk (2), hypertension (1), anemia (1), genetic factors (1), excessive fall risk (1), stroke (1)	Score ≥4
ATRIA Bleeding Risk Score	Anemia (3), eGFR<30 mL/min (3), age ≥75 y (2), history of bleeding (1), hypertension (1)	Score ≥5
HAS-BLED Score	Hypertension (1), abnormal renal (1) or liver (1) function, stroke (1), bleeding (1), labile INR (1), elderly—age >65 y (1), drugs (1) or alcohol (1)	Score ≥3
ORBIT Score	Older age >74 y (1), reduced hemoglobin (2), bleeding history (2), insufficient kidney function (1), treatment with antiplatelets (1)	Score ≥4

American Heart Journal April 2016

Uremic Bleeding: Presentations

Urology and Nephrology Center

- Cutaneous manifestations:
  - Easy bruising
  - Ecchymoses
  - Bleeding from venipuncture site
- Mucosal manifestations:
  - Epistaxis
  - Gingival bleeding
  - Gastrointestinal bleeding
- Intracranial hemorrhage
- Retroperitoneal bleeding
- Hemothorax
- Hemopericardium

Seminars in Dialysis 2006; 19: 317-322

GIT Bleeding

Seminars in Dialysis

Evidence-based Review of Gastrointestinal Bleeding in the Chronic Kidney Disease Patient

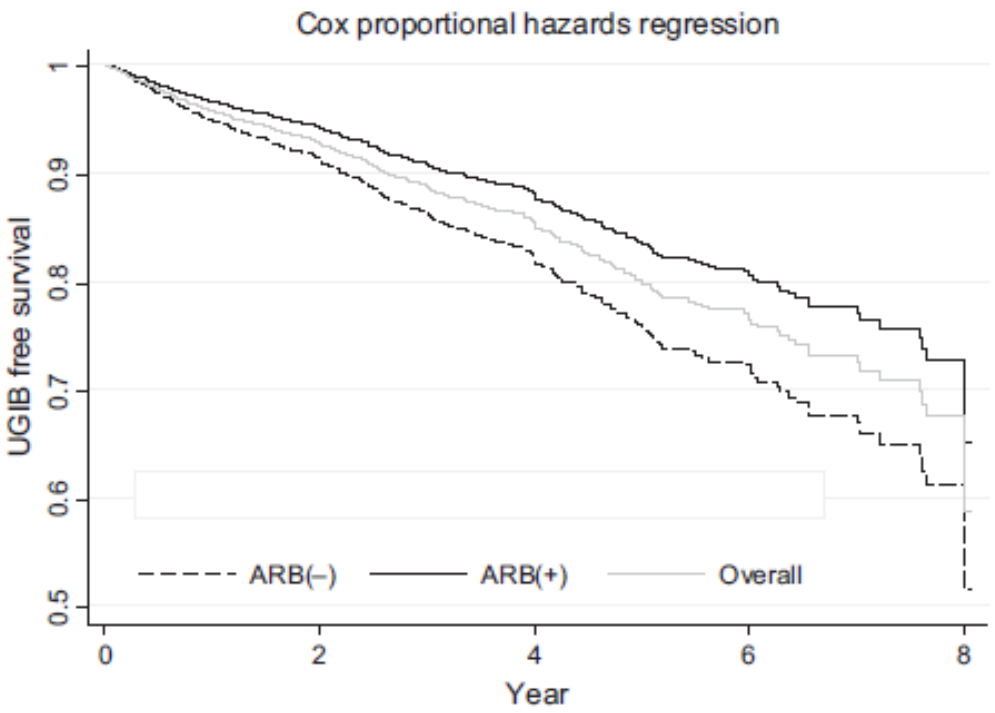
Richard S. Kalman* and Marcos C. Pedrosa†
*Section of Gastroenterology, Department of Medicine, Boston University Medical Center, Boston, Massachusetts, and †Section of Gastroenterology, Department of Medicine, VA Boston Healthcare System, Boston, Massachusetts

Upper GI blood loss: Peptic ulcer disease

Lower GI blood loss: Angioectasia

Gastrointest Endosc 2013;77:609-16.

Upper GI Bleeding: Role of ARBs (n 2744)



Upper gastrointestinal bleeding (UGIB) free survival in hypertensive chronic kidney disease patients with and without angiotensin II receptor blocker (ARB) with adjustments for age, estimated glomerular filtration rate, a history of UGIB, *Helicobacter pylori*, diabetes, cardiovascular disease (CAD), blood urea nitrogen (BUN) and albumin

What's known

Angiotensin II receptor blocker prevents gastric mucosa damage in animal model.

What's new

Angiotensin II receptor blocker decreases risk of upper gastrointestinal bleeding in hypertensive patients with chronic kidney disease and not on dialysis.

Int J Clin Pract, July 2015, 69, 7, 722–728

Uremic Bleeding: Presentations

Urology and Nephrology Center

Accepted Manuscript

Pharmacologic provocation combined with endoscopy in refractory cases of gi bleeding

Daniel L. Raines, MD, Kellen T. Jex, MD, Mark J. Nicaud, MD, Douglas G. Adler, MD

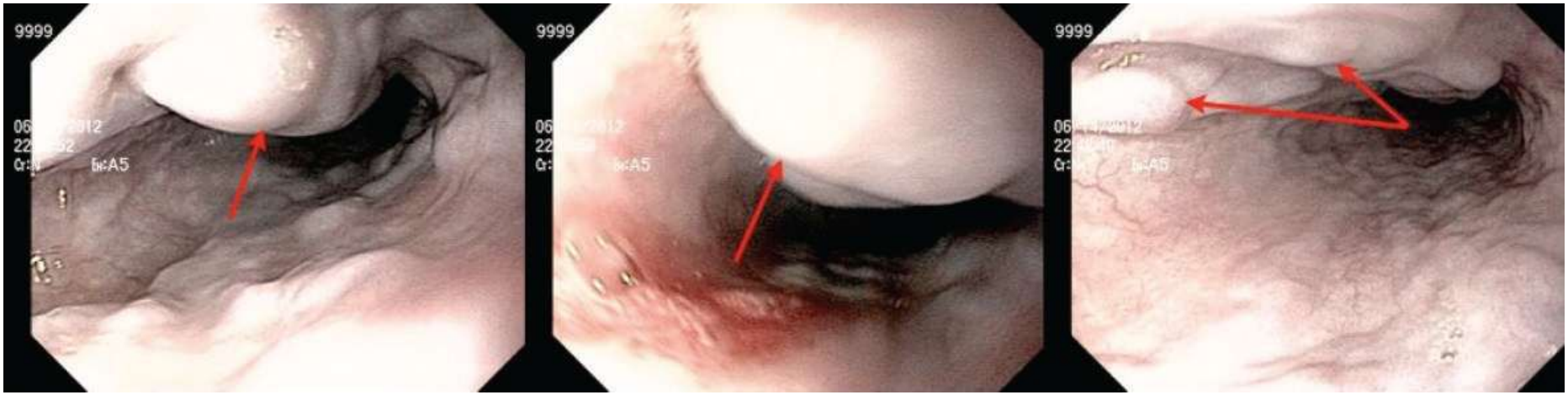
Uremic Bleeding: Presentations

Urology and Nephrology Center

Hindawi Publishing Corporation
Case Reports in Gastrointestinal Medicine
Volume 2013, Article ID 830796, 3 pages
http://dx.doi.org/10.1155/2013/830796

Case Report

"Downhill" Esophageal Varices due to Dialysis Catheter-Induced Superior Vena Caval Occlusion: A Rare Cause of Upper Gastrointestinal Bleeding



Uremic Bleeding: After CABG

Urology and Nephrology Center

Association Between K/DOQI Stage of CKD and Postoperative Bleeding

GFR (mL/min/1.73 m²)	Univariate Analyses			Multivariate Analyses*		
	OR	95% CI	*P*	OR	95% CI	*P*
At risk or stage 1 (GFR ≥ 90)	1.00	(Referent)	—	1.00	(Referent)	—
Stage 2 (GFR 60-89)	1.67	0.85-3.27	0.14	1.55	0.68-3.53	0.30
Stage 3 (GFR 30-59)	3.82	1.78-8.19	<0.001	4.07	1.49-11.11	0.006
Stage 4/5 (GFR <30)	5.60	1.60-19.56	0.007	10.23	2.34-44.78	0.002

*Controlling for age, sex, elective versus nonelective admission mode, highest intraoperative ACT, cardiopulmonary bypass time, baseline hematocrit, and albumin level.

Am J Kidney Dis 2003; 41:84-89.

Access Bleeding

Urology and Nephrology Center

Seminars in Dialysis

ASDIN
AMERICAN SOCIETY OF DIAGNOSTIC AND INTERVENTIONAL NEPHROLOGY

Review

Thrombocytopenia in ESRD Patients: Epidemiology, Mechanisms and Interventional Nephrology Perspective

Ravish Shah,* Nabil Haddad,* Tushar J. Vachharajani,† Arif Asif,‡ and Anil Agarwal*
*Divisions of Nephrology, The Ohio State University, Columbus, Ohio, †W. G. (Bill) Hefner Veterans Affairs Medical Center, Salisbury, North Carolina, and ‡Albany Medical College, Albany, New York

Seminars in Dialysis—Vol 27, No 6 (November–December) 2014 pp. 618–625

Retroperitoneal Hemorrhage

Urology and Nephrology Center

Hindawi Publishing Corporation
Case Reports in Critical Care
Volume 2016, Article ID 5643470, 4 pages

Uremic Bleeding: After Renal Biopsy

AJKD
Original Investigation

Bleeding Complications of Native Kidney Biopsy: A Systematic Review and Meta-analysis

Kristin M. Corapi, MD,[1] Joline L.T. Chen, MD, MS,[2] Ethan M. Balk, MD, MPH,[3] and Craig E. Gordon, MD, MS[2]

Impact of Patient- and Procedural-Related Factors on Erythrocyte Transfusion Rates

	No. of Studies	No. of Procedures	Transfusion Rate (95% CI)	*P* for Difference
SCr				
Categorical				
≥2 mg/dL	9	3,408	2.1 (0.9-3.8)	0.02
<2 mg/dL	10	3,290	0.4 (0.0-1.3)	
Continuous	19	6,698	—	0.08

Am J Kidney Dis. 2012; 60(1):62-73.

Management Algorithm of Uremic Bleeding

Uremic bleeding suspected or confirmed?

Yes

No

DDAVP

Treatment option	Prevents uremic platelet dysfunction	Effective for active bleeding	Useful in males and females	Improves platelet adhesion	Improves platelet aggregation	Increases platelet size or number	Reduces bleeding time	Normalizes bleeding time
Dialysis	+	−	+	−	+	+	++	+
Recombinant human EPO	+	+/−	+	+	+	+	++	+
Cryoprecipitate	−	++	+	−	−	−	++	+
Desmopressin	−	+++	+	−	+/−	−	+++	++
Estrogen intravenous	−	+	+	−	+	−	++	+
Estrogen oral	−	+	+	−	+	−	+	+
Estrogen transdermal	−	+	+	−	−	−	+	−

Yes

No

Monitor hemoglobin and hematocrit and vital signs

Conjugated estrogens regardless of gender

NATURE CLINICAL PRACTICE NEPHROLOGY MARCH 2007

Heparin Free Dialysis: Coated Dialyzers

Urology and Nephrology Center

ARTICLE IN PRESS

AJKD

Original Investigation

Vitamin E–Coated and Heparin-Coated Dialyzer Membranes for Heparin-Free Hemodialysis: A Multicenter, Randomized, Crossover Trial

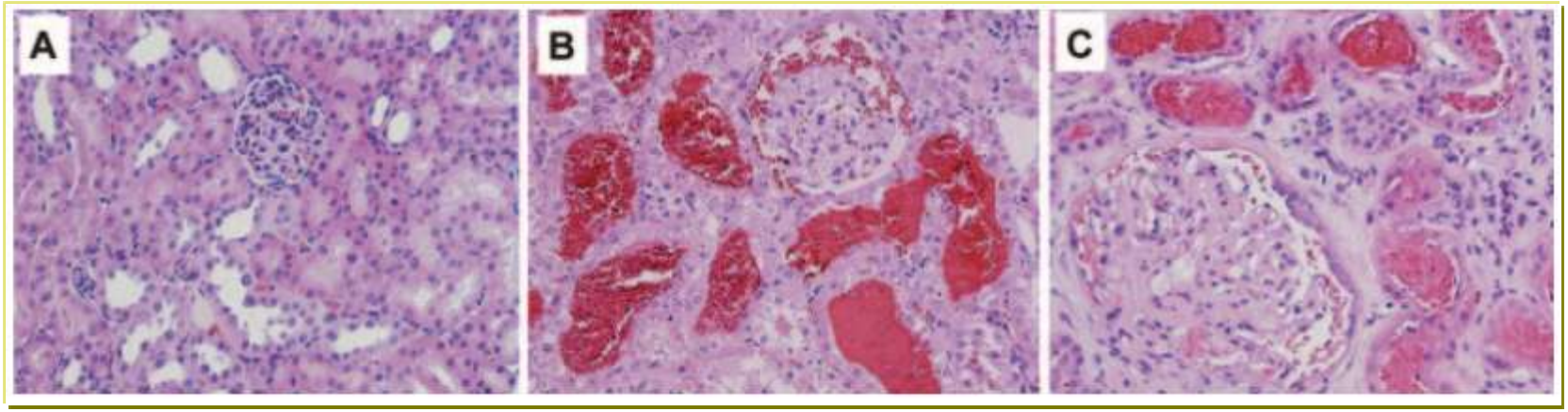
Mohamed Shariful Islam, MBBS,[1] Zarih Alcheikh Hassan, MD,[2] Florence Chalmin, MD,[1] Sandor Vido, MD,[1] Mohamed Berrada, MD,[1] David Verhelst, MD,[2] Patrick Donnadieu, MD,[2] Olivier Moranne, MD, PhD,[1] and Vincent L.M. Esnault, MD, PhD[1,3]

Heparin Free Dialysis: Coated Dialyzers

Urology and Nephrology Center

Am J Kidney Dis. 2016, in press

Anticoagulation Related Nephropathy



J Am Soc Nephrol 22: 1856 –1862, 2011.

Anticoagulation Related Nephropathy

Urology and Nephrology Center

REVIEW ARTICLE

Anticoagulation-related nephropathy

D. S. WHEELER,* R. P. GIUGLIANO† and J. RANGASWAMI*‡

Department of Medicine, Einstein Medical Center, Philadelphia, PA; †Cardiovascular Division, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; and ‡Delaware Valley Nephrology and Hypertension Associates, Philadelphia, PA, USA

Recommended frequency of renal monitoring for patients receiving anticoagulation

		Maintenance		
	Initiation (3 months)	GFR > 60 mL min^{-1}	GFR 30–60 mL min^{-1}	GFR < 30 mL min^{-1}
Warfarin	3–4 weeks	6 months	2–3 months	2–3 months
DOAC	3–4 weeks	12 months	6 months	3 months

J Thromb Haemost. 2016 Mar;14(3):461-7

Anticoagulation Related Nephropathy

Drug Saf (2015) 38:527–533
DOI 10.1007/s40264-015-0290-z

LEADING ARTICLE

Oral Anticoagulants and Risk of Nephropathy

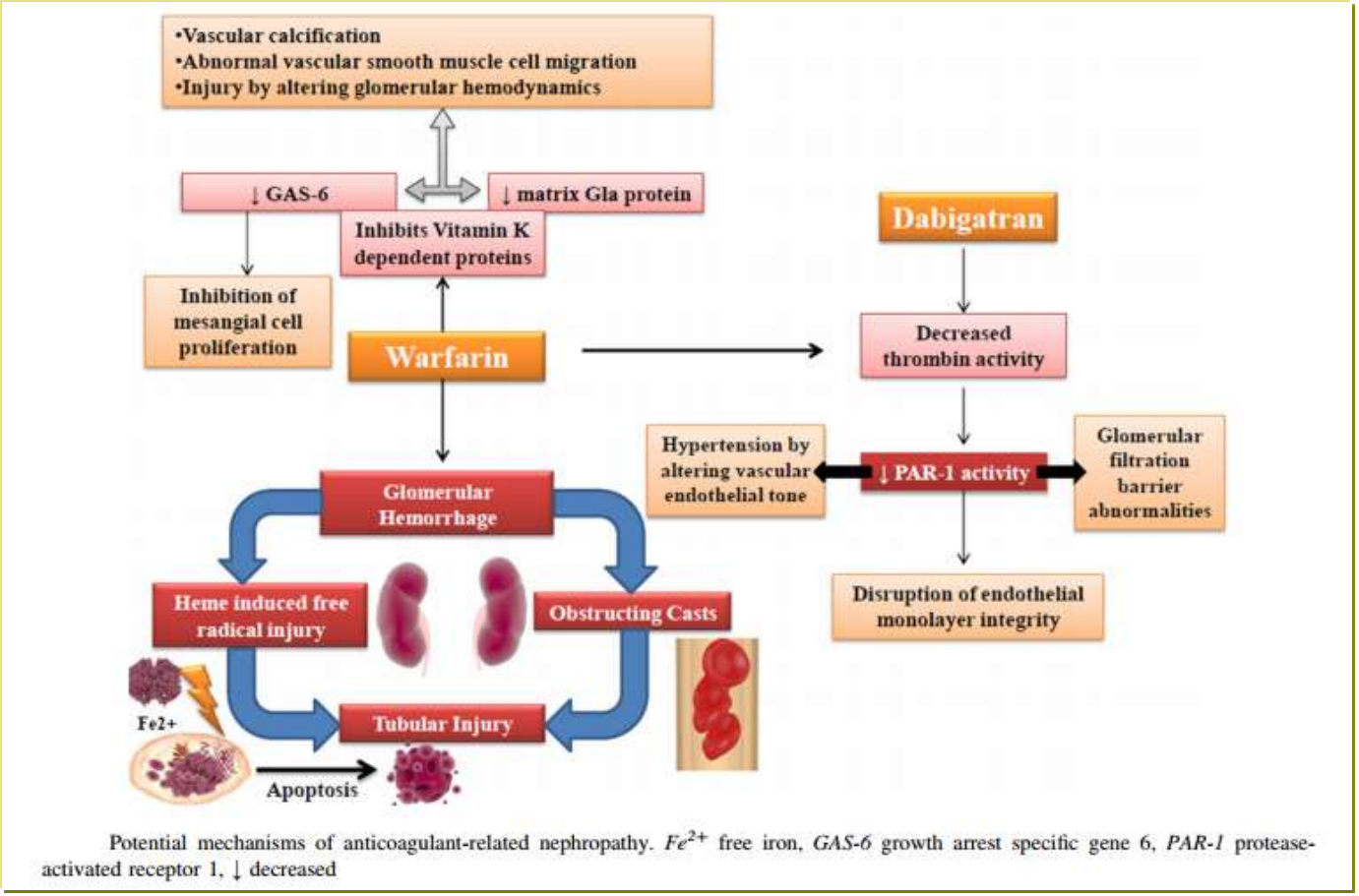
Vinay Narasimha Krishna[1] · David G. Warnock[1] · Nakshatra Saxena[2] · Dana V. Rizk[1]

Risk factors for developing warfarin-related nephropathy
Coagulopathy (INR >3)
Chronic kidney disease
Cardiovascular disease and heart failure
Diabetes mellitus
Simultaneous use of medications such as aspirin, angiotensin converting enzyme inhibitors, and calcium channel blockers
Thin and thick basement membrane disease
Age
Hypertension
Low serum basal albumin level
High serum AST level at post INR elevation
Gene polymorphisms affecting warfarin metabolism (e.g., CYP2C9*3 polymorphism)

AST aspartate aminotrasferase, *CYP* cytochrome P450, *INR* international normalized ratio

Drug Saf (2015) 38:527–533

Anticoagulation Related Nephropathy



Potential mechanisms of anticoagulant-related nephropathy. Fe^{2+} free iron, *GAS-6* growth arrest specific gene 6, *PAR-1* protease-activated receptor 1, ↓ decreased

Drug Saf (2015) 38:527–533

Anticoagulation Related Nephropathy

Urology and Nephrology Center

WARFARIN-RELATED NEPHROPATHY IN A KIDNEY TRANSPLANT PATIENT: Nadeen J. Khoury, Mark A. Perazella, Yale-New Haven Hospital, Yale School of Medicine, New Haven, CT, USA.

NKF 2016 Spring Clinical Meetings Abstracts

Invasive Procedure:
Management of Antithrombotic

Urology and Nephrology Center

Perioperative management of antithrombotic therapy

Agent	Patient Population	Recommendation (Recommendation Grade)
Aspirin	High risk for CV event	Continue aspirin (2C)
	Low risk for CV event	Stop 7–10 d before procedure (2C)
Vitamin K antagonists (*e.g.*, warfarin)	High risk for thromboembolism	Use bridging anticoagulation (2C)
	Low risk for thromboembolism	Stop 5 d before procedure (1C); resume 12–24 h after procedure (2C)
Intravenous UFH as bridging anticoagulation	High risk for thromboembolism	Stop 4–6 h before procedure (2C)
LMWH as bridging anticoagulation	High risk for thromboembolism	Last therapeutic dose 24 h before procedure; for procedures at high risk of bleeding, resume 48–72 h after procedure (2C)

CV, cardiovascular; 2C, weak recommendation on the basis of low-quality evidence; 1C, strong recommendation on the basis of low-quality evidence; UFH, unfractionated heparin; LMWH, low molecular weight heparin.

Clin J Am Soc Nephrol 11: 354–362, February, 2016

Invasive Procedure:
Management of Antithrombotic

Urology and Nephrology Center

n 2619

CHRONIC KIDNEY DISEASE. PATHOPHYSIOLOGY, PROGRESSION & RISK FACTORS - 2

MP257 **RISK FACTORS ASSOCIATED WITH BLEEDING COMPLICATIONS AFTER NATIVE RENAL BIOPSY**

Jennifer S Lees, Emily McQuarrie, Natalie Mordi, Jonathan Fox, Colin Geddes and Bruce MacKinnon

NHS Greater Glasgow and Clyde, Renal Medicine, Glasgow, UNITED KINGDOM

Nephrology Dialysis Transplantation 31 (Supplement 1): i422–i438, 2016

Invasive Procedure:
Management of Antithrombotic

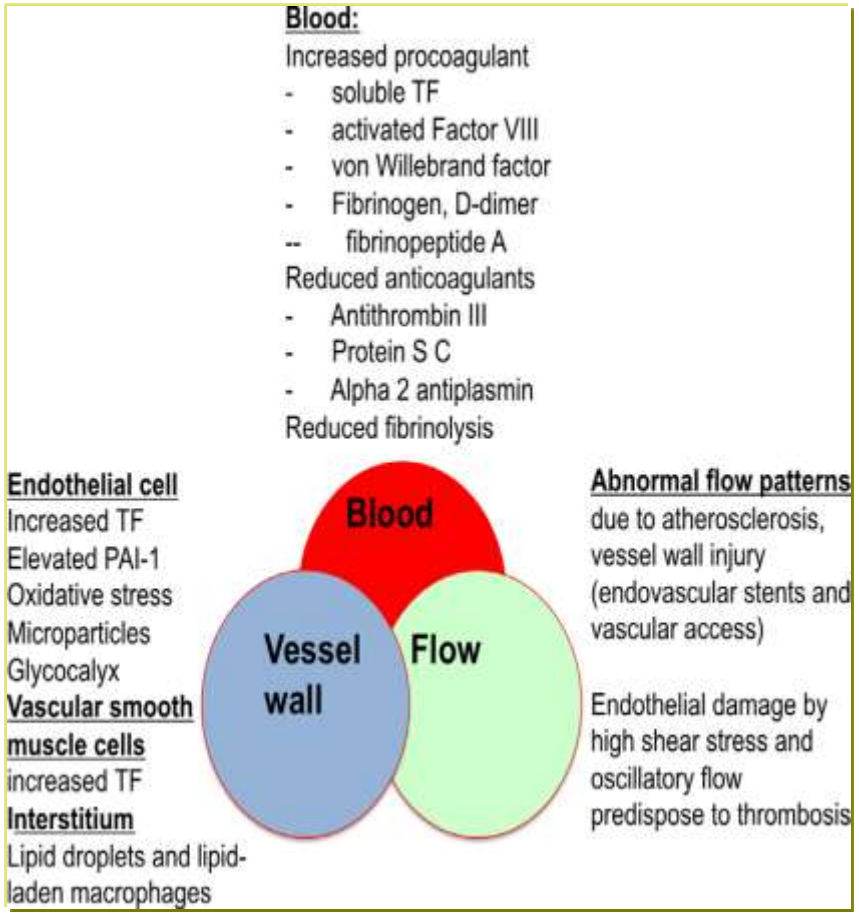
Urology and Nephrology Center

Interruption of Target-Specific Oral Anticoagulant Therapy for Invasive Procedures and Surgery

Drug and CL_{cr}	Time of Last Dose Before Minor Procedure	Time of Last Dose Before Major Surgery
Dabigatran		
>50 mL/min	1 day	2 days
30–50 mL/min	2 days	4 days
≤30 mL/min	4 days	5–6 days
Rivaroxaban, apixaban, or edoxaban		
>50 mL/min	1 day	2 days
30–50 mL/min	1–2 days	3–4 days
≤30 mL/min	2 days	4 days

Am J Health-Syst Pharm. 2016; 73(suppl 2):S5-13

Thromboembolic Risk in Patients with CKD



Seminars in Dialysis—Vol 28, No 2 (March–April) 2015, pp.198–205

How to Predict Stroke?

Urology and Nephrology Center

ation

Congestive
Hypertensio
Age ≥75 y:
Diabetes me
History of st
bolism: 2 po
Vascular dis
tery disease
Age 65-74 y
Sex categor

r thromboem-

peripheral ar-

c

CHA2DS2-VASc score	Patients (*n* = 7329)	Adjusted stroke rate %/ year
0	1	0
1	422	1.3
2	1230	2.2
3	1730	3.2
4	1718	4.0
5	1159	6.7
6	679	9.8
7	294	9.6
8	82	6.7
9	14	15.2

Effect of Renal Dysfunction on AF outcome

G Model
JJCC-1301; No. of Pages 7

ARTICLE IN PRESS

Journal of Cardiology xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Baseline $CHADS_2$, CHA_2DS_2-VAS_c, and HAS-BLED scores according to renal function.

Variable	eGFR ≥60 mL/min (n = 1834)	eGFR <60 mL/min (n = 292)	p value
$CHADS_2$			<0.001
Low (score = 0)	623 (34.0)	34 (11.6)	
Intermediate (score = 1)	633 (34.5)	88 (30.1)	
High (score ≥2)	578 (31.5)	170 (58.2)	
CHA_2DS_2-VAS_c			<0.001
Low (score = 0)	348 (19.0)	9 (3.1)	
Intermediate (score = 1)	483 (26.3)	35 (12.0)	
High (score ≥2)	1003 (54.7)	248 (84.9)	
HAS-BLED			<0.001
Low (score = 0)	292 (15.9)	10 (3.4)	
Moderate (score = 1–2)	1144 (62.4)	137 (46.9)	
High (score ≥3)	398 (21.7)	145 (49.7)	

Thrombophilia: Impact on AVF

Urology and Nephrology Center

Article

Thrombophilia and Arteriovenous Fistula Survival in ESRD

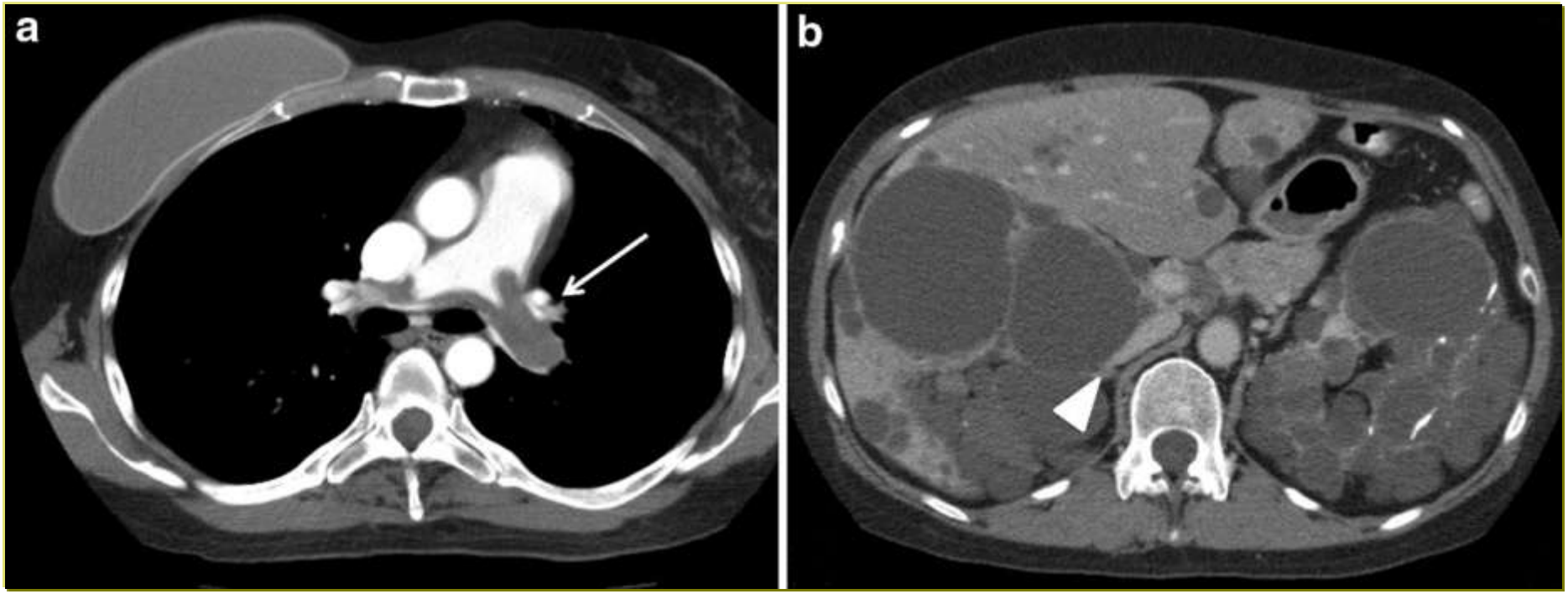
Clin J Am Soc Nephrol 8: 962–968, 2013.

Thromboembolic Risk in Patients with CKD

Age Group (yr)	Pulmonary Embolism Admissions per 100,000 Persons by Kidney Disease Category		
	Normal Kidney Function	CKD	ESRD
20–44	24	137	682
45–54	51	236	367
55–64	80	312	312
65–74	154	220	456
≥75	249	304	462
All	66	204	527

Clin J Am Soc Nephrol 7: 1584–1590, 2012

Thromboembolic Risk and Dialysis



CEN Case Rep (2016) 5:74–77

Stroke and Dialysis

Seminars in Dialysis

Reviews

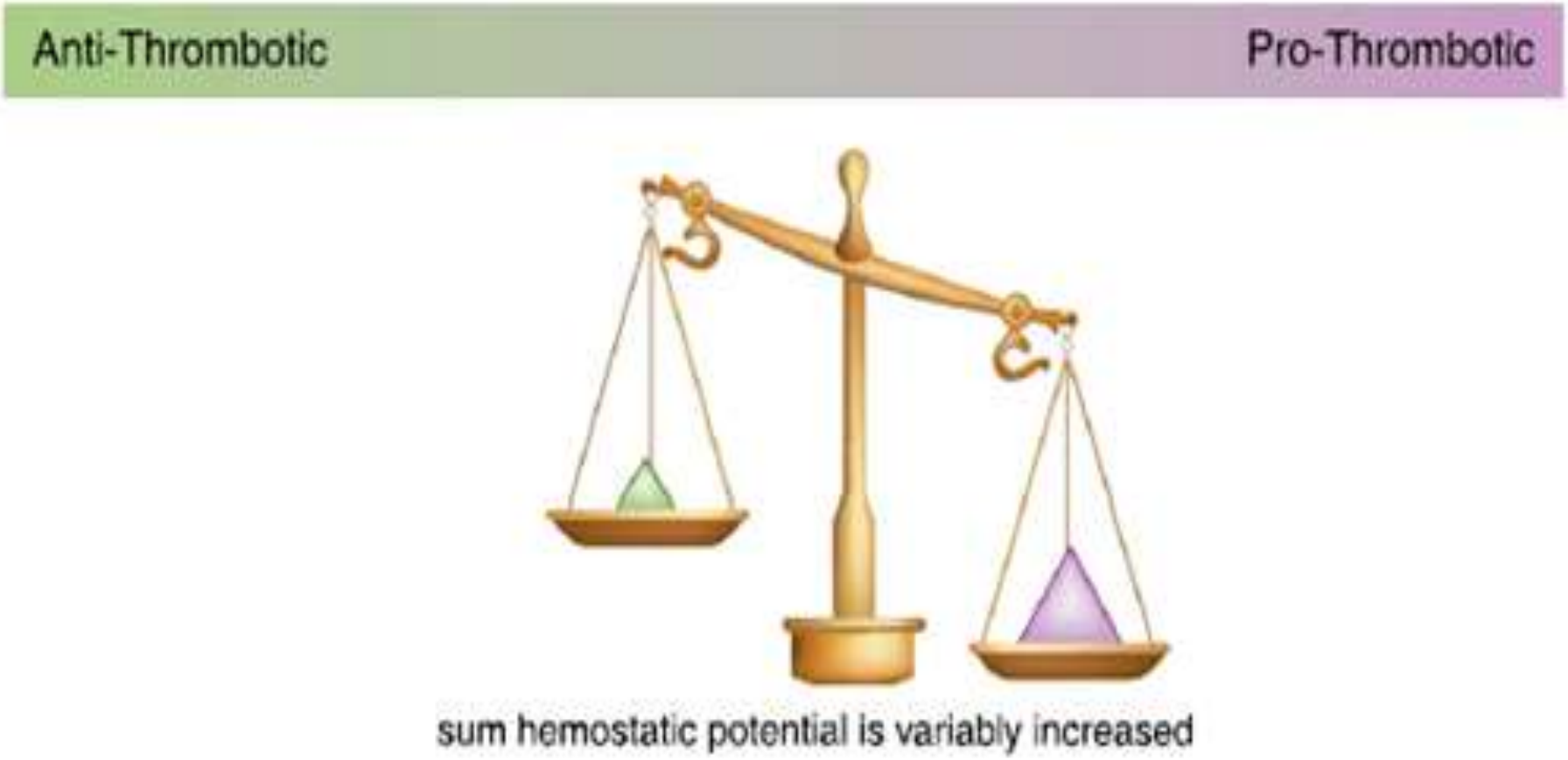
Evidence for the Prevention and Treatment of Stroke in Dialysis Patients

William Herrington,*† Richard Haynes,*† Natalie Staplin,* Jonathan Emberson,* Colin Baigent,* and Martin Landray*

*Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom, and †Oxford Kidney Unit, Churchill Hospital, Oxford University Hospitals NHS Trust, Oxford, United Kingdom

Seminars in Dialysis—Vol 28, No 1 (January–February) 2015, pp. 35–47

Nephrotic Syndrome:
Risk of Thrombosis



Clin J Am Soc Nephrol 7: 513–520, 2012.

Nephrotic Syndrome:
Risk of Thrombosis

Urology and Nephrology Center

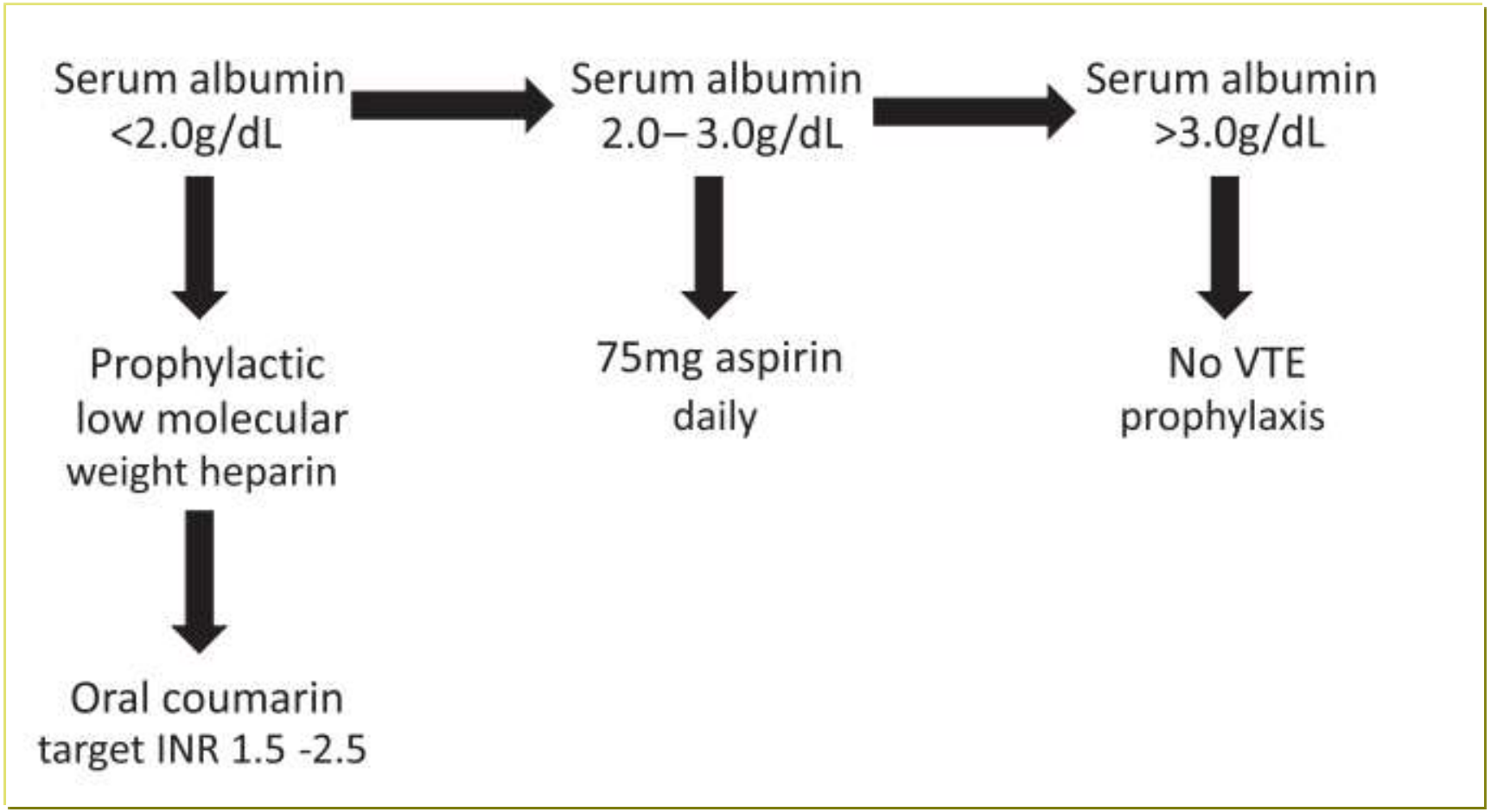
EDUCATIONAL REVIEW

Platelet abnormalities in nephrotic syndrome

Benedicte Eneman[1,2] · Elena Levtchenko[1,2] · Bert van den Heuvel[2] · Chris Van Geet[3] · Kathleen Freson[3]

Pediatr Nephrol (2016) 31:1267–1279

Nephrotic Syndrome:
Use of Prophylactic Anti-thrombotic



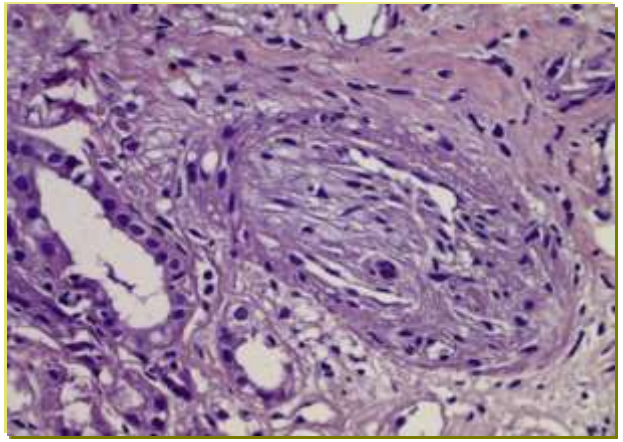
Clin J Am Soc Nephrol 9: 478–483, 2014

Antiphospholipid Syndrome

Urology and Nephrology Center

Renal involvement in primary antiphospholipid syndrome

Vascular lesion	Clinical signs
Renal artery stenosis (trunk or main branches)	Renovascular hypertension (severe)
Thrombosis/occlusion/stenosis	Renal infarction (silent, painful, hematuria)
Renal thrombotic microangiopathy (fibrin thrombi in glomerular capillaries, afferent arterioles, interlobular arteries)	Sistemic hypertension, Renal failure (acute, mild to severe), Proteinuria (mild to nephrotic range)
Fibrous intimal hyperplasia of interlobular arteries; fibrous and fibrocellular thrombosis of arteries and arterioles; arteriosclerosis (cortical atrophy)	Mild proteinuria, renal failure (chronic)
Renal vein thrombosis	Nephrotic syndrome, renal failure (if bilateral)



J Nephrol (2016) 29:507–515

Choice of Anticoagulation

Urology and Nephrology Center

Characteristic	Drug choice	Rationale
Mechanical valve or valvular atrial fibrillation	Warfarin	New agents not studied
Liver dysfunction with increased INR	Warfarin	New agents require hepatic metabolism
Poor compliance	Warfarin or nothing*	Missed doses of greater consequence with shorter-acting new agents
Stable on warfarin	Warfarin	Consider switching at patient request
CrCl less than 30 mL/min	Warfarin	Such patients were excluded from trials with new agents
CrCl of 30-50 mL/min	Rivaroxaban or apixaban	Oral factor Xa inhibitors are less affected by impaired renal function than dabigatran
Dyspepsia or upper gastrointestinal symptoms	Rivaroxaban or apixaban	Dyspepsia in up to 10% given dabigatran
Recent gastrointestinal bleed	Apixaban	More gastrointestinal bleeding with dabigatran (150 mg twice daily) or rivaroxaban than with warfarin
Recent ischemic stroke on warfarin	Dabigatran	Dabigatran (150 mg twice daily) associated with lower risk of ischemic stroke than warfarin
Recent acute coronary syndrome	Rivaroxaban or apixaban	Small myocardial infarction signal with dabigatran
Poor compliance with twice-daily dosing or request for a once-daily regimen	Rivaroxaban	Only agent given once daily

CrCl indicates creatinine clearance.
*For some patients who are not adherent to instructions, the risk of any anticoagulant therapy may outweigh any benefits

Hematology Am Soc Hematol Educ Program 2012;2012(1):536-540.

Choice of Anticoagulation

Urology and Nephrology Center

Barriers to anticoagulation adherence	Warfarin	DOACs
1. Therapy-related factors		
Regular INR monitoring and dose adjustment	Issue	Issue addressed to an extent: no INR monitoring required, but elderly patients and patients with renal impairment require regular kidney function tests and dose is adjusted accordingly
Dietary requirements		
(a) Dietary vitamin K restriction	Issue	Issue addressed
(b) Ingestion of medication after meals to facilitate drug absorption and bioavailability, or to ameliorate gastrointestinal adverse effects	Not an issue	Might be an issue with both rivaroxaban and dabigatran
Drug–drug interaction	Issue	Dabigatran has relatively low potential for interaction with concomitant medications, but issue not completely resolved
Drug–alcohol interaction	Issue	Issue not addressed
Restricted physical activities	Issue	Issue not addressed
Pill burden (more than once daily dosing)	Not an issue	Issue with dabigatran and apixaban
Absence of antidote	Not an issue	Issue with rivaroxaban and apixaban
2. Patient-related factors		
Memory capacity	Issue	Issue not resolved
Attitude towards risk–benefit of therapy	Issue	Issue not addressed
3. Condition-related factors	Issue	Issue not addressed
4. Social–economic factors		
Medication cost	Not an issue	Dependent on drug subsidy policies in different countries
Costs involved in clinical appointments and laboratory tests	Dependent on the distance to clinics, frequency of appointments and laboratory tests	Not an issue
5. Health system-related factors	Issue	Issue not addressed

Patient
DOI 10.1007/s40271-016-0180-1

REVIEW ARTICLE

Factors Affecting Patients' Perception On, and Adherence To, Anticoagulant Therapy: Anticipating the Role of Direct Oral Anticoagulants

Ekta Y. Pandya[1] · Beata Bajorek[1,2]

Published online: 20 July 2016

Anticoagulation in ESRD

Urology and Nephrology Center

Anticoagulation guidelines in ESRD patients with AF

Scientific society (reference)	Year	Guideline
K-DOQI	2005	Antithrombotic therapy (warfarin and aspirin) should be considered, based on an assessment of the risk of embolism and of bleeding complications. Dialysis patients are at increased risk for bleeding and careful monitoring should accompany intervention.
KDIGO	2011	Weighing the available evidence, the benefit of warfarin anticoagulation for primary prevention of stroke in CKD 5D patients is questionable.
European Society of Cardiology	2012	AF patients with severe renal failure have not been adequately studied and their risk assessment is complex.
Canadian Society of Cardiology	2014	There are no randomized trials data for nonvalvular AF patients who are dialysis dependent, and we therefore cannot recommend their routine anticoagulation.
American Heart Association/ American College of Cardiology/Heart Rhythm Society	2014	For patients with nonvalvular AF with a CHA2DS2-VASc score of ≥2 and who have end-stage CKD (creatinine clearance <15 mL/min) or are on hemodialysis, it is reasonable to prescribe warfarin (INR 2.0-3.0) for oral anticoagulation. (*Level of Evidence: B*)

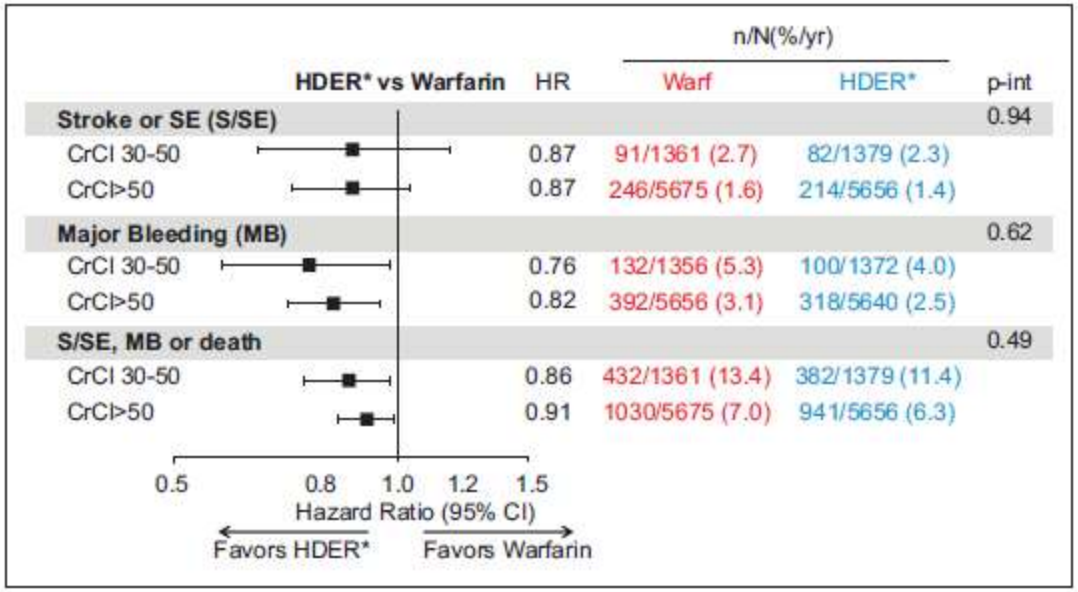
American Heart Journal April 2016

Anticoagulation in CKD

ORIGINAL RESEARCH ARTICLE

n 14 071

Impact of Renal Function on Outcomes With Edoxaban in the ENGAGE AF-TIMI 48 Trial



Circulation. July 2016;134:24-36

Anticoagulation in Dialysis

Urology and Nephrology Center

Seminars in Dialysis

DRUG THERAPY: SPECIAL CONSIDERATIONS IN DIALYSIS PATIENTS

Pharmacokinetic properties of anticoagulants in renal failure

	Normal half-life	Half-life in renal dysfunction*	Plasma protein binding (%)	Renal excretion (%)
Heparin	1–2 hours	1–2 hours	High	10
Enoxaparin	5–7 hours	6–9 hours	High	40
Dalteparin	2–5 hours	4–8 hours	High	
Tinzaparin	1–2 hours	5 hours	High	
Fondaparinux	17–21 hours	>21 hours	94	77
Argatroban	39–51 minutes	0.5–1 hour	54	16
Bivalirudin	25 minutes	3.5 hours	None	20
Warfarin	1 week	1 week	99	92
Dabigatran	12–17 hours	28 hours	35	80
Rivaroxaban	5–9 hours	10 hours	92–95	36
Apixaban	12 hours	17 hours	87	27
Edoxaban	9–11 hours	10–14 hours	60	35

*half-life values will vary depending on the degree of renal dysfunction

Seminars in Dialysis—Vol 28, No 4 (July–August) 2015, pp. 354–362

Anticoagulation in Dialysis

Urology and Nephrology Center

Dabigatran and Rivaroxaban Use in Atrial Fibrillation Patients on Hemodialysis

Kevin E. Chan, MD MSc[1,2], **Elazer R. Edelman, MD PhD**[3,4], **Julia B. Wenger, MPH**[1], **Ravi I. Thadhani, MD MPH**[1], and **Franklin W. Maddux, MD**[2]

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[4]Cardiovascular Medicine Division, Brigham and Women's Hospital, Boston, MA

Circulation. 2015 March 17; 131(11): 972–979.

Anticoagulation in Dialysis

AJKD

Original Investigation

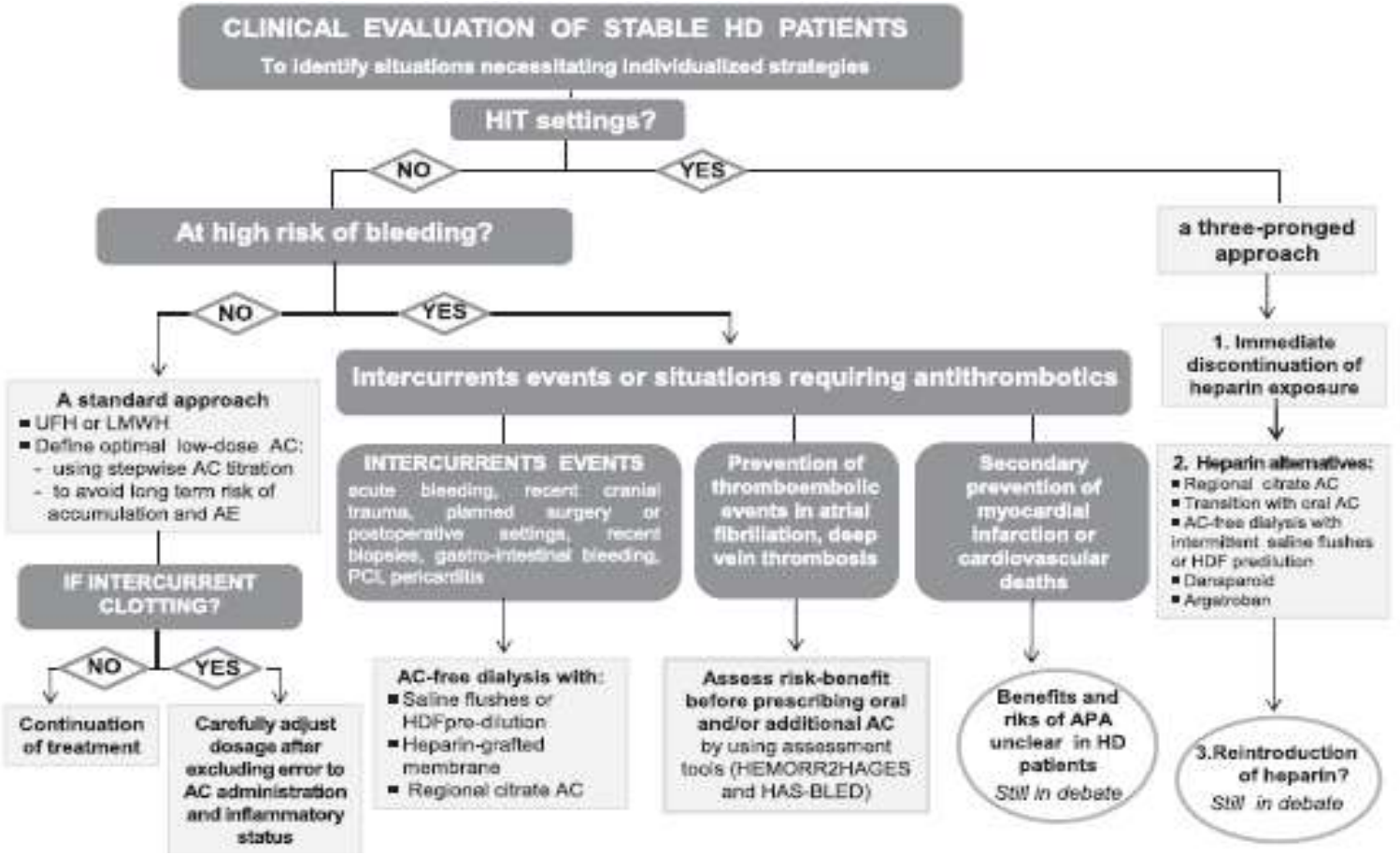
Dose-Finding Study of Rivaroxaban in Hemodialysis Patients

An S. De Vriese, MD, PhD,[1] Rogier Caluwé, MD,[2] Els Bailleul, MD,[3] Dirk De Bacquer, PhD,[4] Daniëlle Borrey, PhD,[5] Bruno Van Vlem, MD, PhD,[2] Stefaan J. Vandecasteele, MD, PhD,[1] and Jan Emmerechts, MD, PhD[5]

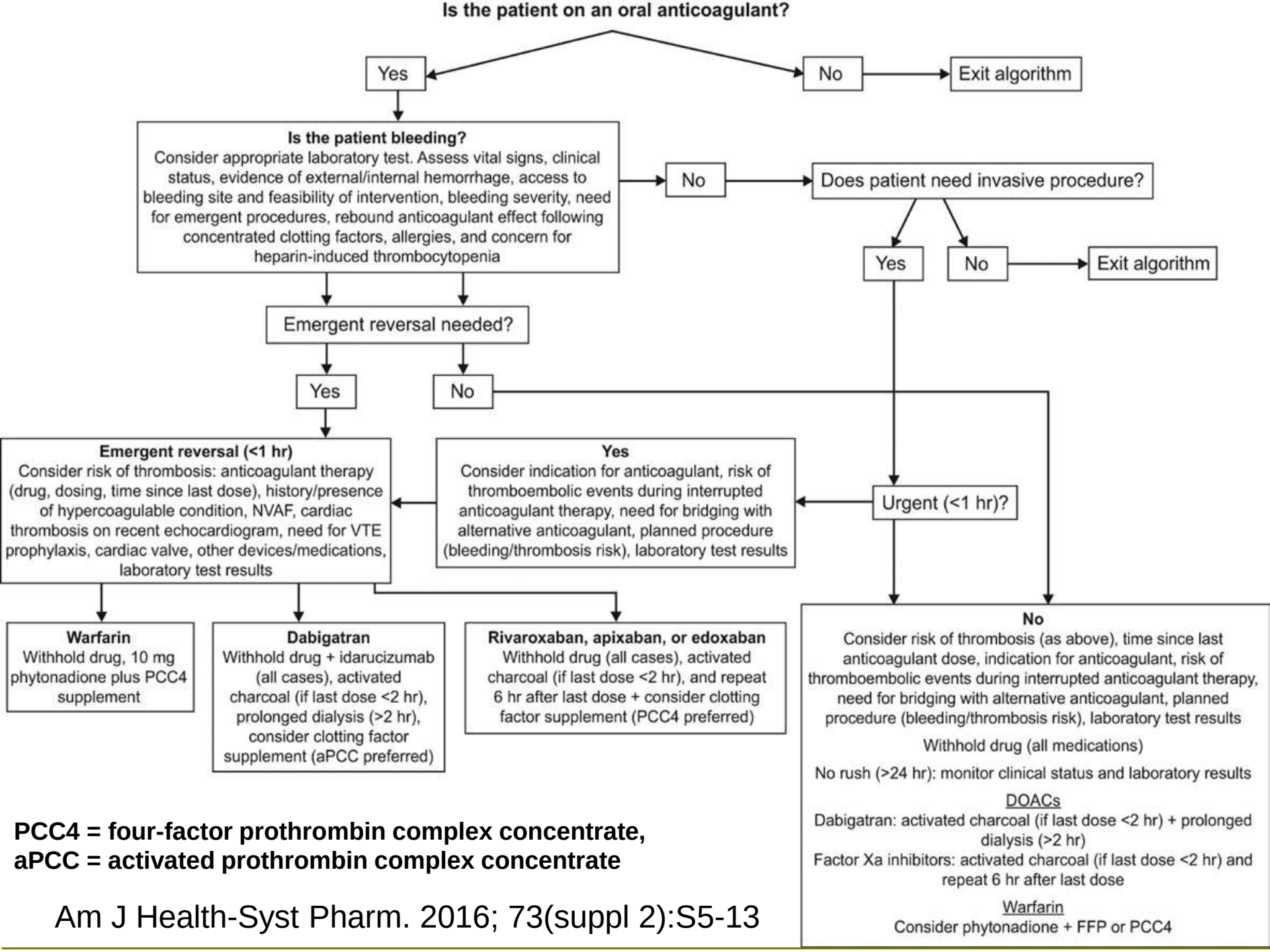
Am J Kidney Dis. 2015;66(1):91-98

Anticoagulation in Dialysis

Urology and Nephrology Center



Seminars in Dialysis—Vol 28, No 5 (September–October), 2015 pp. 474–489



PCC4 = four-factor prothrombin complex concentrate,
aPCC = activated prothrombin complex concentrate

Am J Health-Syst Pharm. 2016; 73(suppl 2):S5-13

Clopidogrel in CKD

Urology and Nephrology Center

Seminars in Dialysis

Clopidogrel Use in End-Stage Kidney Disease

Bassem Y. Tanios,* Houssam S. Itani,† and Deborah L. Zimmerman†‡
*Nephrology Department, Paris Sud University, Le Kremlin Bicêtre, France, †Division of Nephrology, Department of Medicine, University of Ottawa, Ottawa Hospital, Ottawa, Ontario, Canada, and ‡Kidney Research Centre of the Ottawa Hospital Research Institute, Ottawa, Ontario, Canada

Seminars in Dialysis—Vol 28, No 3 (May–June) 2015, pp. 276–281

Pharmacogenomics

Cardiovascular Pharmacogenomics—Implications for Patients With CKD

Larisa H. Cavallari and Darius L. Mason

Cardiovascular Gene-Drug Pairs With the Most Evidence to Date

Gene(s)	Drug	Current State of the Evidence and Considerations in Kidney Disease
CYP2C19	Clopidogrel	• CYP2C19 poor and intermediate metabolizer phenotypes are associated with reduced response to clopidogrel and an increased risk for major adverse cardiovascular events with clopidogrel treatment after PCI compared to the extensive and ultrarapid metabolizer phenotypes. • CPIC guidelines recommend alternative treatment with prasugrel or ticagrelor after an acute coronary syndrome and PCI in CYP2C19 poor and intermediate metabolizers in the absence of contraindications. • The FDA-approved clopidogrel label contains a boxed warning about reduced clopidogrel efficacy with the poor metabolizer phenotype. • Although no dose adjustment is necessary for prasugrel or ticagrelor in patients with kidney disease, patients with end-stage kidney disease may be at higher risk for bleeding with these agents and thus need close monitoring.

Advances in Chronic Kidney Disease, Vol 23, No 2 (March), 2016: pp 82-90

Thrombolome

Urology and Nephrology Center

Seminars in Dialysis

ASDIN
AMERICAN SOCIETY OF DIAGNOSTIC AND INTERVENTIONAL NEPHROLOGY

Review

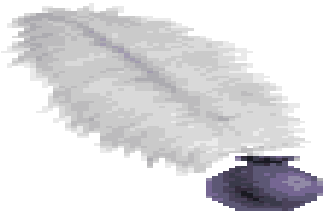
Thrombosis in the Uremic Milieu—Emerging Role of "Thrombolome"

Moshe Shashar, Jean Francis, and Vipul Chitalia
Renal Section, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts

Seminars in Dialysis—Vol 28, No 2 (March–April) 2015, pp.198–205

Hemostasis in Uremia:
Bleeding Diathesis Vs. Hypercoagulability

Urology and Nephrology Center



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